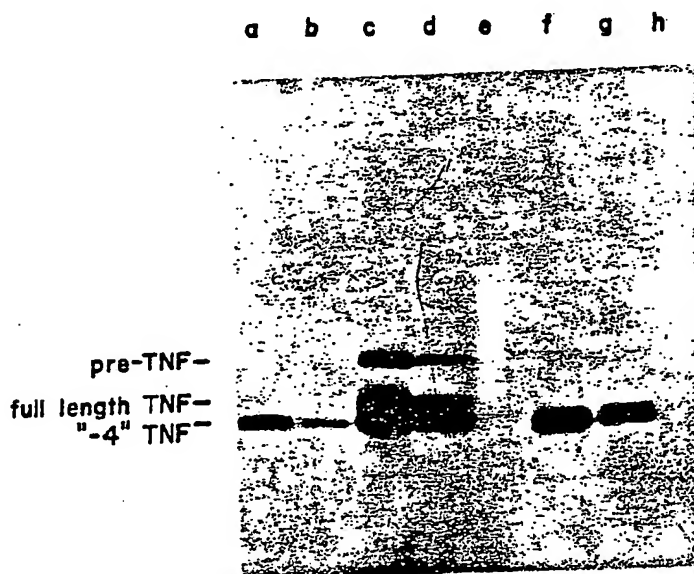




INTERNATIONAL APPLICATION PUBLISHED UNDER THE PATENT COOPERATION TREATY (PCT)

(51) International Patent Classification ⁴ : C12N 15/00, 1/20	A1	(11) International Publication Number: WO 88/ 07079 (43) International Publication Date: 22 September 1988 (22.09.88)
(21) International Application Number: PCT/US88/00374 (22) International Filing Date: 8 February 1988 (08.02.88) (31) Priority Application Number: 023,637 (32) Priority Date: 9 March 1987 (09.03.87) (33) Priority Country: US (71) Applicant: CETUS CORPORATION [US/US]; 1400 Fifty-Third Street, Emeryville, CA 94608 (US). (72) Inventors: CHANG, Shing ; CHANG, Shen-Yung ; 2289 Manzanita Drive, Oakland, CA 94611 (US). (74) Agent: HALLUIN, Albert, P.; Cetus Corporation, 1400 Fifty-Third Street, Emeryville, CA 94608 (US).		(81) Designated States: AT (European patent), AU, BE (European patent), CH (European patent), DE (European patent), DK, FI, FR (European patent), GB (European patent), IT (European patent), JP, LU (European patent), NL (European patent), NO, SE (European patent). Published With international search report.

(54) Title: EXPRESSION OF HETEROLOGOUS GENES IN STREPTOMYCES SPECIES



(57) Abstract

Vectors effective for the expression and secretion of heterologous genes in streptomycetes are disclosed. Such vectors comprises a plasmid replicable in *Streptomyces*, which comprises a *Streptomyces* promoter and a DNA sequence encoding a *Streptomyces* signal sequence operably linked to, and under control of the promoter, which DNA sequence encoding a *Streptomyces* signal sequence may be operably linked to a heterologous gene encoding a desired protein so that the *Streptomyces* signal sequence and heterologous protein are expressed, and the desired protein is secreted under control of the *Streptomyces* signal sequence. Various *Streptomyces* promoters and secretion signal sequences may be used in the invention, and DNA sequences comprising the promoters operably linked to DNA sequences encoding *Streptomyces* signal sequences, are disclosed as part of the invention. Vectors comprising the *Streptomyces aph*, *ermE*, *ermEal* and modifications thereof, controlling the expression of the *amy* and ORF438 signal sequences, which lead to secretion of desired heterologous proteins when transformed into *Streptomyces* hosts, are exemplified.